REMARKS

Claims 18 and 20-27 are pending. Claims 18 and 27 have been amended. Claim 26 has been withdrawn from further consideration. Claims 18, 20-25, and 27 stand rejected. Reconsideration of the claims in light of the following remarks is requested.

Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections made by the Patent Office. Applicants reserve the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional applications.

Claim Amendments

Claims 18 and 27 have been amended for technical clarity. Support may be found at page 3, line 14 to page 4, line 7; and page 70, lines 18-25.

Claim Objection

Claim 18 was objected to because of an informality. Specifically, the Examiner suggests that term "the voltage" should be changed to "a voltage." Claim 18 has been amended to correct this informality. Applicants respectfully request withdrawal of this objection.

Claim Rejection Under 35 U.S.C. § 103

Claims 18, 20, 24 and 27 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Sigal *et al.* (U.S. 6,319,670) ("*Sigal*") in view of Meade *et al.* (U.S. 5,770,369) ("*Meade*") and Roberts *et al.* (U.S. 5,958,791) ("*Roberts*").

Claim 21 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over *Sigal*, in view of *Meade*, and *Roberts*, as applied to claims 18, 20, 24 and 27, and further in view of Bamdad *et al.* 5,620,850) ("*Bamdad*").

Claim 22 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over *Sigal* in view of *Meade*, and *Robert.*, as applied to claims 18, 20, 24, and 27, and further in view of Gerpheide *et al.* (U.S. 5,565,658) ("*Gerpheide*").

Claim 23 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over *Sigal* in view of *Meade* and *Roberts* as applied to claims 18, 20, 24, and 27, and further in view of Kayyem *et al.* (U.S. 6,096,273) ("*Kayyem*").

Claim 25 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over *Sigal* in view of *Meade* and *Roberts* as applied to claims 18, 20, 24, and 27, and further in view of *Kayyem*.

The Applicant respectfully disagree.

When rejecting claims under 35 U.S.C. §103, the Examiner bears the burden of establishing a prima facie case of obviousness. See, e.g., *In re Bell* 26 USPQ2d 1529 (Fed. Cir. 1993); M.P.E.P. Section 2142. To establish a *prima facie* case, three basic criteria must be met: (1) the prior art reference(s) must teach or suggest each and every limitation of the rejected claims; (2) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine their teachings; and (3) there must be a reasonable expectation of success. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not in Applicants' disclosure. *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991); M.P.E.P. §2142.

A. Overview of the disclosure of *Sigal*, *Meade*, and *Roberts*.

1. *Sigal* *Sigal* is directed to compositions and methods used to measure the presence of analyte by measuring electrochemiluminescence triggered by a voltage imposed on a working electrode. *See* col. 1, lines 15 – 19 and lines 48-49. It further discloses that such electrochemiluminescence is measured with a photomutiplier tube (PMT). *See* col. 17, lines 26-27. It also discloses compositions and methods for conducting electrochemiluminescence binding

assays using microparticles that include electrically conductive material. *See* Abstract. As acknowledged by the Examiner, *Sigal* does not disclose "an array of working electrodes" and "a detector capable of detecting a voltage associated with electron transfer from said electron transfer moiety."

2. *Meade* *Meade* is directed to electron transfer via nucleic acids. *See* col. 1, lines 11-12. It discloses that electronic detection is used, including voltammetry. *See* col. 27, lines 3-4.

3. *Roberts* *Roberts* discloses a test device for detecting or determining an analyte in a test solution. The device includes a electrochemical measurement portion comprising two conductors. Each conductor comprises a plurality of fingers, and the two sets of fingers are interdigitated to form an "array". *See* Abstract and FIG. 2. The electrochemical measurement portion is located at one end of an absorbent material, the other end of which is dipped into a solution. There is a liposome lysing portion and a competitive binding portion located between the measurement portion and the solution contact end. *See* FIG. 1.

Roberts also discloses a method of detecting an analyte in a sample with the device using marker-encapsulating liposomes. Upon lysis when migrated through a lysing portion of the device, the liposome releases the marker, which is correlated to the amount of analyte presented. The electroactive marker will be in contact with the two conductors to complete the electric circuit and the current flowing between the two conductors is correlated to the presence or amount of the analyte in the sample. *See* col. 5, line 60, to col. 6, line 65.

Roberts discloses that the advantages of fabricating small electrodes in interdigitated "arrays" include allowing redox cycling of ions back and forth between anode(s) and cathode(s). This generates larger currents for detection and allows for the use of small sample volumes. *Roberts* also discloses that microelectrodes fabricated in an interdigitated "array" have advantages due to the ease of ionic diffusion. *See* col. 8, lines 2-8.

B. The references do not teach "an array of working electrodes".

Claims 20-25, and 27 depend on claim 18, which recites "an array of working electrodes".

As presented above, neither *Sigal* nor *Meade* disclose "an array of working electrodes." This defect is not cured by *Roberts*.

The instant application discloses that by electrode "is meant a composition, which, when connected to an electronic device, is able to sense a current or charge and convert it to a signal. Alternatively an electrode can be defined as a composition which can apply a potential to and/or pass electrons to or from species in the solution. " *See* page 11, lines 10 – 13.

In contrast, *Roberts* discloses a first conductor with fingers that interdigitate with fingers of a second conductor. *See* col. 16, lines 17-19. *Roberts* then refers to such fingers as "electrodes" and uses the terms such as "interdigitated electrode arrays". *See* col. 7, line 66 and col. 16, line 14-17. However, because the fingers are connected together to form part of the conductor, a person skilled in the art will understand that such fingers are not individual electrodes; the conductors as a whole, including the fingers, are electrodes. As the Examiner will appreciate, each electrochemical cell requires a working (indicator) electrode and at least a second counter electrode to complete the circuit. (Note that in the present invention, there is an array of working electrodes and usually only a single counter electrode. *See* page 77, lines 10-19). The two "conductors" of *Roberts* are a working electrode and a counter electrode. In fact, *Roberts* describes a "four-electrode" system as comprising "the interdigitated array, a reference electrode, and an auxiliary electrode", thus indicating that the interdigitated array is the working and counter electrode. *See* col. 23, lines 30 – 33. For this reason, *Roberts* does not actually disclose an array of working electrodes. It only discloses a set of interdigitated fingers that make up a single working electrode and a counter electrode. *See* col. 16, lines 14-20 and FIG. 2. Therefore, *Roberts* only discloses a set of electrodes with interdigitated fingers but not "an array of working electrodes" as claim 18 recites.

C. There is no motivation to combine *Roberts* with any of the other references because the suggested combination will render the device disclosed in *Roberts* unsatisfactory for its intended purpose.

If proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984) MPEP 2143 .1.

As more fully explained below, *Roberts* does not teach electrodes comprising binding ligands. Applicants submit that any modification to *Roberts*-type electrodes by adding binding ligands will render it unsatisfactory for its intended purpose. A person skilled in the art would understand that covering the conductors with biological substance, such as binding ligands, will shield the conductors from the solution surrounding it. As such, the current between the conductors will be impeded and the redox cycling of ions back and forth between anode(s) and cathode(s), as *Roberts* discloses, will be hindered. It would also impede the ionic diffusion disclosed by *Roberts*.

Moreover, in rejecting claim 20, the Examiner suggests that *Roberts* can be combined with *Sigal* because *Sigal* discloses a plurality of colloids comprising a self-assembled monolayer ("SAM"). Applicants similarly submit that such a combination also will render the device disclosed in *Roberts* unsatisfactory for its intended purpose.

A person skilled in the art will understand that if the conductors in *Roberts*' device are covered with a SAM, it will not carry current easily. As the present application discloses:

> when the SAM is on the electrode, a monolayer serves to keep charge carriers away from the surface of the electrode. Thus, this layer helps to prevent direct electrical contact between the electrode and charged species within the solvent. Such contact can result in a direct "short circuit" or an indirect short circuit via charged species which may be present in the sample. Accordingly, the monolayer is preferably tightly packed in a uniform layer on the electrode surface, such that a minimum of "holes" exist. The monolayer thus serves as a physical barrier to block solvent accesibility to the electrode. Page 48, lines 2-8.

For this reason, the conductors, if covered by either binding ligand or SAM, or both, as the Examiner suggests, it would likely impede the reaction, and would hinder redox cycling of ions back and forth between anode(s) and cathode(s) because the binding ligands and SAM serve as barrier to block the current. Thus, the conductors would not work properly and be unsatisfactory for *Roberts*' intended purpose.

D. It is improper to combine *Roberts* with other references because *Roberts* teaches away from the instant invention.

Furthermore, it is improper to combine references where the references teach away from their combination. In *re Grasselli*, 713 F.2d 731, 743, 218 USPQ 769, 779 (Fed. Cir. 1983). A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be led in a direction divergent from the path that was taken by the applicant. *In re Gurley*, 27 F.3d 551, 553, 31 USPQ2d 1130, 1131 (Fed. Cir. 1994).

Claims 20-25, and 27 depend on claim 18, which includes the "electrode comprises a binding ligand" requirement.

As presented above, *Roberts* discloses conductors with interdigitated fingers. It also discloses binding materials that specifically bind to the analyte. *See* col. 11, lines 29-41. However, *Roberts* teaches that "binding material" is not to be attached to the electrode.

Roberts discloses methods of detecting analyte using the device it disclosed. There are two formats of detection: a competition format and an aggregation format. In either format, there are marker-loaded liposomes coupled with an analyte analogue, *see* col. 22, lines 13-15 and col. 22, lines 38-40, and there is "binding material" that can bind to the analyte or analyte analogues. *See* col. 11, lines 29-40. In the competition format, the binding material is bound to the absorbent material in the competitive binding portion, which is between the electrochemical measurement portion and the contact portion. *See* col. 22, lines 12-35. Alternatively, *Roberts* discloses an embodiment where the competitive binding portion is replaced with a capture binding portion that has a capture probe binds to it. *See* col. 10, lines 49-55.

In the aggregation format, the binding material is in an aqueous, electrolytic medium, to form part of a test mixture. The binding material will react with the conjugate in the absence of the analyte, to form aggregates. When the analyte presents, it will bind to the binding material. *See* col. 22, lines 48-67.

Therefore, in either format, the binding material is located away from the conductors/electrodes. In the competition format the binding material is bound to the competitive binding portion of the test strip; and in an alternative embodiment, the binding material is bound the capture portion of the test strip. Both the competitive binding portion and the capture portion are located apart from the electrode. In the aggregation format the binding material is not bound at all, but rather is in the test mixture. Therefore, *Roberts* discloses that the binding material is not associated with the electrode. A person skilled in the art, upon reading *Roberts*, will take a route opposite to what the claimed invention requires - the binding ligand to be associated with the electrode.

E. The teachings of the references are not sufficient to render the claims *prima facie* obvious because the proposed combination with or modification of *Sigal* would change the principle of operation of *Sigal*.

As presented above, *Sigal* does not disclose a voltage detector. It discloses only measuring electrochemiluminescence with a PMT. Nevertheless, the Examiner asserts that to modify the PMT of *Sigal* with the voltage detector of *Meade* is a "simple replacement." Applicants respectfully disagree.

As stated in MPEP 2143.01, if the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious. *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959).

Sigal is directed to compositions and methods for the detection of labels that emit an electrochemiluminescent signal upon a triggering by voltage imposed on a working electrode. As

such, the principle of operation of *Sigal* is based on optical detection of light and not on the measurement of a change in voltage. Thus, replacing the optical detector in *Sigal* with the voltage detector of *Meade* is not a "simple replacement" – because it totally changes the operation principle of *Sigal*. Therefore, teachings of the references are not sufficient to render the pending claims *prima facie* obvious.

F. There is no reasonable expectation to success because modification of *Roberts* will render it inoperable

As presented above, covering the conductors disclosed in *Roberts* with binding ligands and SAMs should impede the current between the electrode and hinder redox cycling of ions back and forth between anode(s) and cathode(s) because the binding ligands and SAM serves as physical barriers, which block the current.

For the forging reasons, the Examiner failed to establish a *prima facie* case of obviousness. Therefore, claim 18, and claims 20-25, and 27, which depend thereon are not obvious in view of *Sigal* and *Meade* over *Roberts*; Claim 21 is not obvious over *Sigal*, in view of *Meade*, and *Roberts*, and further in view of *Bamdad*; Claim 22 is not obvious over *Sigal* in view of *Meade*, and *Robert.*, and further in view of *Gerpheide*; and Claims 23 and 25 are not obvious over *Sigal* in view of *Meade* and *Roberts*, and further in view of *Kayyem*. Applicants respectfully request the rejections to be withdrawn.

CONCLUSION

Applicants respectfully submit that the claims are now in condition for allowance and early notification to that effect is respectfully requested. If the Examiner feels there are further unresolved issues, the Examiner is respectfully requested to phone the undersigned at (415) 781-1989.

Respectfully submitted,
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